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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,257	10/26/2001	Yves Delmotte	WM-267.00	3743

7590 08/30/2005

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EXAMINER	
SILVERMAN, ERIC E	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 08/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/004,257	DELMOTTE, YVES	
	Examiner	Art Unit	
	Eric E. Silverman, PhD	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *14 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10-28-02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant should note that the Examiner assigned to this application has changed. **The Examiner currently assigned to this application is Eric Silverman, PhD**, whose phone number can be found near the end of this Office Action.

Receipt of the following documents is hereby acknowledged: Applicant's response to Examiner's Election/Restriction Requirement, filed 6/14/2005, and Authorization to Act in a Representative Capacity, filed 7/14/2005.

In Applicant's response to Examiner's Election/Restriction Requirement, Applicant elected with to prosecute the invention of Group I, claims 1 – 28, and further elected fibrin as the material that composes the biopolymer or biomembrane. Applicant did not argue the error in the restriction of Group V from Groups I – IV. Therefore, the restriction is deemed to be without traverse with respect to Group V. Applicant also did not argue the error in restricting Groups I and II from Groups III and IV. Thus, with respect to the restriction of Groups I and II from Groups III and IV, the election is also deemed to be without traverse. Applicant also did not traverse the requirement to elect a single species for the biomaterial, which forms the membrane. Applicant did traverse the restriction between Group I and Group II, and the restriction between Group III and Group IV. This traverse is addressed below.

Response to Arguments

Upon consideration, Group I and II have been rejoined by the examiner.

Applicant's arguments that Group III should be examined with Group IV are not pertinent at this time, since Applicant did not elect either of these groups. Nonetheless,

Applicant's arguments were fully considered, and found to be unpersuasive. Both groups are drawn to membranes with different chemical compositions, one requires thrombin and one does not. Simply because two groups are in the same class and subclass does not necessarily mean that the search for both will coextend. In this case, since the composition of the groups may be the different, the search for both compositions will not coextend, and therefore the search of both in one application would constitute a burden on the Office. As such, restriction for examination purposes is proper. Claims 1 – 31 are pending in this action. Claims 32 – 72 are withdrawn from consideration as drawn to non-elected inventions.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 – 9, 15, and 17 – 26, and 29 – 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Delmotte et al., US 5,989,215.

Applicability of US 5,989,215 as Prior Art

It is recognized that Applicant is claiming benefit of parent applications Serial Number 09/566372 (now US 6,599,515 B1), however there is no support in this application for the limitations a thickness less than about 75 microns, a solvent concentration less than about 5% by weight of the membrane, a radius of curvature of

less than about 5 centimeters, or a maximum pore size of about 20 microns recited in claim 1 of instant Application. Applicant is also claiming benefit of parent application 9386198 (now US 6,461,325 B1). However, there is no support in parent Application for recited limitation curvature of less than about 5 centimeters recited in instant claim 1. It is also recognized that Applicant is claiming benefit of parent Application 08679658 (now US 5,989,215). However, there is no support in parent Application for recited limitation curvature of less than 5 centimeters recited in instant claim 1.

As such, instant Application is not afforded benefit of the parent Applications, and the filing date of instant application is 10/20/2001, and US Patent 5,989,215 is therefore a competent prior art reference. See *In re* Scheiber 192 USPQ 782.

Reason for Rejection of Instant Claims

US 5,989,215 (hereafter '215) teaches a fibrin membrane composed mainly of fibrinogen, thrombin, factor XIII and calcium (column 5, lines 14 – 16). '215 specifically envisages a film with two or more layers wherein one is the barrier membrane and one layer is another, rigid fibrin layer that provides rigidity to the structure (column 6, lines 28 – 34), or in a "sandwich" structure with two fibrin layers, one of which is a membrane and one of which is a biomaterial (example 8). The pore size of the membrane barrier is below 20 microns, below 5 microns and below about 1 micron (column 6, lines 5 – 8), and where the thickness of the barrier is between 20 and 2000 microns (column 6, lines 35 – 40). The fibrin that forms the membrane and the polymer is taught to be composed mainly of fibrinogen, thrombin, factor XIII and calcium (column 5, lines 14 – 16). The inventors also specifically propose that the material can

be obtained by combining fibrinogen and thrombin and then activating them to form cross linked fibrin (column 7, lines 55 – 65). Thus, the taught thrombin is deemed to be activable, as recited in claims 21 – 22. The thrombin is further taught to be prepared from plasma (column 7, lines 29 – 31), and is therefore deemed to be natural, as recited in claims 19 – 21. '215 also specifically suggests the use of t-PA, streptokinase, and other firbinolytic agents (column 7, lines 15 – 18) in order to control the rate of degradation of the membrane in the body. Since the materials are taught and demonstrated for use in a living subject (examples 5 –8), a person of ordinary skill in the art would understand that it must be sterile. '215 teaches a method of making this product by applying two liquid solutions to the body part to be treated, which then react to form the product (see examples 1 – 8). 215 also suggests using the layers of the product taught by '215 that are not the membrane layers as a drug delivery system.

The only element that is not expressly taught or specifically suggested by instant reference is a radius of curvature or less than 5 centimeters. However, it would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to make the product of instant claims with this radius of curvature. The disclosed use of the product is to aid in wound healing by forming a barrier to prevent adhesions, for example between tissue layers, in the body of a subject. Thus, the artisan, when making the product, would make it in the correct shape to correspond to the shape of the body part that was being treated by use of the product. If the shape of the body part to be treated was substantially flat, or had a radius of curvature of less than 5

centimeters, then the artisan would find it obvious to make the product to fit this specification. Since the product is taught to be able to be made from liquid solutions that react to form the product, the liquid solutions could be applied directly to the body part to be treated, and then the product would form in the correct shape. Therefore, it would be well within the skill of the artisan, in following the teachings of the prior art, to make the product with any desired radius of curvature, and the person of ordinary skill in the art would have a reasonable expectation of success at such manipulations.

Claims 27 – 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,989,215 as applied to claims 1 – 9, 15, 17 - 26 and 29 – 31 above, and further in view of Sierra et al., of record.

The teachings of '215 are discussed above. '215 does not teach pore sizes of about 0.1 microns or about 0.01 microns.

Sierra teaches that the pore sizes of fibrinous materials can be controlled by the artisan. Sierra further teaches that altering the pore sizes will change the mechanical properties of the product.

Thus, it would be prime facie obvious to the person of ordinary skill in the art to make the product '215 with pore sizes of about 0.1 microns or about 0.01 microns. The motivation to do so is to adjust the mechanical properties to obtain maximum benefit. Because Sierra teaches that such manipulations are within the skill of the art, the artisan would have a reasonable expectation of success.

Claims 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,989,215 as applied to claims 1 – 9, 15, 17 - 26 and 29 – 31 above, and further in view of US 4,344,190 (hereafter '190).

The teachings of '215 are discussed above. '215 does not teach the use of a glycerol, dimethyl sulfoxide, or trehalose.

'190 teaches a fibrin product with glycerin. '190 further teaches that glycerin acts as a plasticizer for fibrin (colum 2, lines 46 – 48).

Thus, it would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to add glycerin to the product of '215, thus obtaining the product of instant claims. The motivation would be to improve the mechanical properties of the fibrinous product of instant claims. This is an inherent teaching of '215, since adding a plasticizer is well known in the art to be a method of imparting on a product desirable mechanical properties.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,989,215 as applied to claims 1 – 9, 15, 17 – 26 and 29 - 31 above, and further in view Redl et al, of record.

The teachings of '215 are discussed above.

Redl teaches the use of fibrin film in a drug delivery system with an antibiotic, and that the combination of the two provides both the sealing effect of the film and the therapeutic activity of the antibiotic. Furthermore, Redl shows that the fibrin seal is not adversely affected by the addition of the antibiotic.

Thus, it would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to use an antibiotic in the product of '215. Addition of a drug is expressly suggested by '215, and Redl further motivates this by showing that antibiotics can have therapeutic activity in the presence of fibrin. The expected result of this combination would be a fibrin product with antibiotic activity. The artisan would have a reasonable expectation of success at such manipulations, since Redl shows that antibiotics do not adversely affect the properties of the fibrin film.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,989,215 as applied to claims 1 – 9, 15, 17 - 26 and 29 – 31 above, and further in view of US 3,919,414 (hereafter '414).

The teachings of '215 are discussed above.

'215 does not teach the use of a radioactive marker, specifically a radioactive iodine isotope.

'414 teaches the use of a radioactive isotope of iodine along with fibrin, and the use of said combination as a component in an assay to determine the effectiveness of agents that accelerate the lysis of blood clots (Examples 1 – 4). '414 further teaches that the making of this combination is well known in the art.

Thus, it would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to use radioactive iodine with the product of '215. The motivation to do so comes from '414, which teaches that the use of a radioactive iodine isotope with fibrin films imparts a new utility on the films, namely the use as a diagnostic agent.

Since such is taught to be well known in the art, the skilled artisan would have a reasonable expectation of success at these manipulations.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,989,215 as applied to claims 1 – 9, 15, 17 - 26 and 29 – 31 above, and further in view of US 5,674,488 (hereafter '488).

The teachings of '215 are discussed below. '215 does not teach the use of satins or stanols.

'488 teaches that fibrin clots are linked with heart attacks (column 3, lines 34 – 40). '488 also teaches that statins can be administered to lower the risk of a heart attack (column 4, lines 25 – 27, note that the named drugs are statins).

Thus, it would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to include a statin with the product of '215. '215 expressly suggests using the product as a drug delivery device. Since fibrin clots are linked to heart attacks, it would be obvious to a person of ordinary skill in the art to include a drug that would serve to counteract this effect along with a fibrinous wound-healing product, and statins are examples of such drugs. Since it was specifically contemplated that the product of '215 would act as a drug delivery device, a person of ordinary skill in the art would have a reasonable expectation of success at such manipulations.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,989,215 as applied to claims 1 – 9, 15, 17 - 26 and 29 – 31 above, and further in view of US 5,585007 (hereafter '007).

The teachings of '215 are discussed above.

'215 does not teach the use of the compounds mentioned in instant claim.

'007 teaches that it is aprotinin is typically added to the fibrinogen component of fibrin films used for wound healing, and that such is useful for wound healing (column 22, lines 11 – 17).

Thus, it would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to add aprotinin to the composition of '215, thus making the claimed invention as a whole obvious over the prior art. The motivation for doing so is taught by '007, which teaches that this is a common practice in the art that is generally preformed by the skilled artisan in order to obtain specific benefits, namely increased wound healing benefits. Since this is taught to be a common practice in the art, the artisan would have a reasonable expectation of success.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. WO/25838 has similar content as US 5,989,215, and could have been relied on for rejections of some of the claims of instant application.

No claims are free of the prior art. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric E. Silverman, PhD whose telephone number is 571 272 5549. The examiner can normally be reached on Monday to Friday 9:00am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 571 272 0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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